ASynopsis ReportSubmitted

On

Formulation and evaluation of anti-diabetic polyherbal formulation for the treatment of diabetes

By

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DECLARATION

I hereby declare that this synopsis report submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which to a substantial extent has been accepted for the award of any other degree or diploma of the university or other institute of higher learning, except where due acknowledgment has been made in the text.

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INTRODUCTION

From ancient times, Ayurveda, Siddha, and Unani systems of medicine have dominated India's rich cultural history of traditional medicine, which includes two more extensively practised systems as well[1, 2]. In addition to preserving the traditional legacy, the development of these traditional medical systems with the consideration of safety, efficacy, and quality will also assist justify the use of natural products in healthcare[3]. There is still a lot of original paperwork about the more organised medical systems that have been used by humans since the dawn of time[4]. The market for health-related goods has been active, and these goods are produced in various countries and distributed globally. To guarantee the availability of a uniform product throughout the world, standardisation is required. Standardization guarantees a stronger product with guaranteed ingredients every time[5].

Hyperglycemia, the high blood glucose level (hyperglycemia) brought on by insulin deficiency in diabetes mellitus, is a long-term metabolic disorder that frequently coexists with insulin resistance. The majority of people with diabetes have non-insulin dependent diabetes mellitus, which is a heterogeneous group that includes a milder form of the disease that mostly affects adults[6].

Type 1 and type 2 diabetes are increasing in prevalence globally; 171 million individuals were predicted to have the disease in 2000, and by 2030, that figure is expected to double.[7]

Diabetic retinopathy is categorised as:

1. Cellular devastation (IDDM or Type 1 diabetes)
    a. Immune-mediated disease;
    b. Iidiopathy
2. Insulin resistance (also known as NIDDM or Type 2 diabetes)

A heterogeneous metabolic disorder called diabetes causes hyperglycemia as a result of insufficient insulin secretion, action, or both[8]. It is characterised by altered carbohydrate, lipid, and protein metabolism. It is one of the refractory diseases that the ICMR has identified as requiring treatment with alternative medicine. The prevalence of diabetes mellitus is rising in the modern world[9]. Almost 20 million people in India already have diabetes, and by the year 2025, that figure is expected to rise to 57 million[10].

The current generation of oral hypoglycemic medications cause unwanted side effects[11]. So, there has been a lot of attention in recent years regarding the antidiabetic potential of medicinal plants and their herbal composition in the management of disease.Here, we've included a few medicinal plants with reported antidiabetic properties along with their putative mechanisms of action.

The idea of polyherbalism is unique to Ayurveda, despite the fact that it is challenging to express in terms of contemporary parameters. The principle of synergism behind polyherbal compositions is highlighted in the Sarandghar Samhita. Fundamental elements for medicine formulation are found in ayurveda. The herbs are chosen based on the ailment, and additional herbs are utilised to counteract any negative side effects from the main herb. Given that different herbal preparations have differing degrees of strength and that they work through various mechanisms, it is theoretically plausible that different combinations of these extracts will work better at lowering blood sugar[12]. To take advantage of synergism and discover an appropriate anti-diabetic and anti-oxidant combination therapy, it is customary in the traditional system of plant medicine to utilise plant formulations and combined extracts of plants rather than separate ones. Here, our attention is focused on the potential of various polyherbal formulations that have undergone scientific verification, which show the greatest promise for being relatively safe and effective.

Polyherbalism, a term used to describe the use of more than one herb in a phytotherapy formulation to increase therapeutic efficacy, is flourishing. It is necessary for a herb to either

target the therapeutic activity to a receptor or to enhance the ADME of the other herbs in order to achieve the synergistic effect[13-15].

More than 800 therapeutic herbs, some of which were very helpful in DM, were recorded by ethnobotanical knowledge[16]. The majority of these plants are also found in India, where rural communities continue to use them traditionally[17]. In order to scientifically validate their effectiveness against DM and to discover a replacement for the current anti-diabetic medications, which are notorious for their severe side effects, the medicinal herbs have been thoroughly examined over the past two decades[18]. Recent studies suggest that these plants can lower blood sugar levels through a variety of mechanisms, including the regeneration of pancreatic beta cells, increased insulin secretion and glucose uptake, activation of insulin receptors, and inhibition of glucosidase, amylase, and sodium-glucose transport protein 2 (SGLT2)[19-20]. In addition to being utilised as crude diabetes medications, purified chemicals from these plants, such as berberine, mangiferin, curcumin, stevioside, and capsaicin, have also been investigated for their antidiabetic action and found to be more potent than their source extracts [21-22].

The purpose of the current investigation is to formulate and evaluate anti-diabetic herbal formulation for the treatment of diabetes and collect the preclinical and clinical trials data.

FORMULATION REVIEW

List of materials and equipment's used

- For the fulfillment of the above aim and objectives, the following materials and equipment's will be used.

List of Ingredients[23-39]:

S. No.	Ingredients	Dose	Possible mechanism of action
1.	Gurmar Leaf (Gymnema Sylvestre)	500-1000 mg/*day*	It reduces blood sugar levels by enhancing the level of insulin in the body.
2.	Jamun Seed (Syzygium Cumini)	1000 mg/*kg*	Lower blood sugar while simultaneously blocking the alpha glucosidase enzyme.
3.	Tulsi Leaf (Ocimum Sanctum)	300 mg– 1000 mg/day	Hypoglycaemic and hypolipidemic effect
4.	Karela Seeds (Momordica Charantia)	150 mg/kg/*day*	Reduce blood glucose level
5.	Methi Seeds (Trigonella Foenum-Graecum)	100 mg/kg/*day*	Decrease blood glucose concentration
6.	Cinnamon (Cinnamomum Verum)	200-1200 mg/*kg*/*day*	Lowers plasma glucose level
7.	Guava Leaf (Psidium Guajava)	400-1000 mg/*kg*/*day*	Lowers plasma glucose level
8.	Mango Leaf (Mangifera Indica)	250 mg/*kg*/*day*	Intestinal reduction of glucose
9.	Neem Leaf (Azadirachta Indica)	250 mg/*kg*/*day*	Reduce blood glucose level
10.	Aloe (Aloe Barbadensis)	300 mg/*kg*/*day*	Maintains glucose homeostasis
11.	Green Tea (Camellia Sinensis)	100-200 mg/kg/*day*	Hypoglycemic activity
12.	Vinca Leaf (Vinca Rosea)	500 mg/kg/*day*	Alpha glucosidase inhibitors
13.	Vinca Flower (Vinca	500 mg/kg/*day*	Alpha glucosidase inhibitors

	Rosea)		
14.	Jalkumbhi (Eichhornia)		Lowers the plasma glucose level
15.	Vansh Lochan (Bambusa Arunadinacea)	100-300 mg/kg/*day*	Lowers the plasma glucose level
16.	Jaiphal (Myristica Fragrans)	500 mg/kg/*day*	Lowers the plasma glucose level
17.	Javitri (Myristica Fragrans)	500 mg/kg/*day*	Lowers the plasma glucose level
18.	Choti Elaichi (Elettaria Cardamomum)	250 mg/kg/*day*	Reduce blood glucose level
19.	Alsi Seeds (Linum Usitatissimum)	200 mg/kg/*day*	By modulating
20.	Lady Finger (Abelmoschus Bammia)	100-300 mg/*kg*	Lowers plasma glucose level
21.	Insulin Plant Leaf	250 mg/kg/day	

For the preparation and evaluation of herbal products requires a variety of equipment's such as –

- Double cone blender
- Microscope
- pH meter
- Muffle furnace
- Drying oven
- Hot air oven
- Water bath
- Hot plate
- U V– Spectrophotometer
- Balance and etc.

LITERATURE REVIEW

1. **Kumar et al (2022)**explained the Indian traditional medical system, diabetes is treated with a combination of the herbs Artemisia roxburghiana,Roylea cinerea, Cissampelos pareira, Stephania glabra, Tinospora sinensis, Drimia indica and Curcuma longa. The current study's objective was to construct a polyherbal formulation (PHF) using seven herbs and examine the SGLT2 inhibitory impact in type 2 diabetic rats. The Sarangdhar Samhita, an old Ayurveda treatise that encouraged the use of numerous herbal brews for enhanced therapeutic effects, served as the model for this strategy.

2. **Nasreenet al (2020)**evaluate the ability of Myristica fragrans seed extract to lower blood sugar levels in vivo when given to Swiss albino mice along with glimepiride. In order to compare this combination to the one containing glimepiride and pioglitazone in terms of the binding affinities of the ligands to the respective target protein receptors and the relative stability of the drug-protein complexes, computational tools were used to further validate the in vivo results.Both in alloxan- and glucose-induced hyperglycemia Swiss albino mice, the combined therapy's effects were seen. The Student's t test was used to assess and statistically analyse the average fasting blood glucose levels of the test groups. Compared to glimepiride alone, the combination therapy considerably and time-dependently lowered the blood glucose level.

3. **Azizet al (2019)** was formulatedpolyherbal powder for diabetes mellitus, and its organoleptic, rheological, physical, and phytochemical properties were assessed. The polyherbal powder was made from a variety of herbs. The evaluations were carried out using accepted procedures.The polyherbal powder's organoleptic characteristics were determined to be a dull brown colour, distinctive odour, astringent taste, and a reasonably fine texture. Using phytochemical qualitative analysis, the presence of alkaloids, terpenoids, flavonoids, steroids, tannins, carbohydrates, and glycosides was determined.The polyherbal powder had prolonged stability and good flow characteristics,

according to physicochemical examination. Consequently, the polyherbal powder that may be used to treat diabetes mellitus was assessed.

4. **Tripathi et al (2013)** was concluded that ayurvedic formulations are used for the treatmentof wide variety of diseases including DM. The current study reports on the standardisation of some herbal anti-diabetic drugs as a reference standard for standardisation of the anti-diabetic medications in a quality control laboratory, one option is to use the Limitations derived from the various Physicochemical Characteristics of the eight unique herbal medicines and the marketed formulations.

AIM AND OBJECTIVE

Aim for developing anti-diabetic herbal formulation for the treatment of diabetes

- Comfort to patient.
- Ease of handling
- Ease of manufacture.
- Lack of explosion.
- Possibility of providing a better efficacy.
- Suitable for administration
- Better therapy.

In comparison with the traditional allopathic preparation, it presents some advantages such as

- Potential of better efficacy, a decrease in systemic side effects, and a consequent decrease in unfavourable consequences.
- More economicalas compare to conventional medicine and easier to obtain than prescription medicine.
- Stabilizes hormone and metabolism.
- Natural recovery.
- Fewer side effects.

PLAN OF WORK

STAGE 1)

- REVIEW OF LITERATURE
- Literature Survey
- Review of articles

STAGE 2)

- PREFORMULATION STUDIES
- Solubility Profile
- Melting Point
- Stability analysis

STAGE 3)

- FORMULATION AND OPTIMIZATION METHODS
- Preparation by selected method
- Box behnken design
- Factorial Design

STAGE 4)

- PHYSICAL PROPERTIES
- Organoleptic Evaluation
- Powder fineness and sieve size
- Flow properties

STAGE 5) CHARACTERISATION

- Extractive Values
    - Water and Alcohol Soluble

- Physicochemical Properties
    - Moisture Content
- Ash Values
- Phytochemical screening of the components of different herbal formulation
- In-vitro evaluation of herbal formulation
- In-vivo evaluation of herbal formulation
    - Preclinical
    - Clinical
        - Therapeutic indices and safety margins

EXPECTED OUTCOMES

Herbal diabetes medications are far superior to allopathic ones. DM is thought to be incurable based on the results of global research conducted to date, but it can be treated with the help of a few drugs, both modern and conventional.

Herbal medication is seen as a safer alternative for treating DM and has been used in several traditional medical systems since ancient times. Moreover, a combination of herbs produced better results with less toxicity than a single herb, possibly as a result of the synergistic interaction of the various constituents in these plants. Many polyherbal formulations have undergone extensive research over the past few years, and many of them have been found to be successful in reducing hyperglycemia in various experimental types.

The assessment of a plant sample's toxicity is an important step in carrying out pharmacological experiments in higher models. These investigations assist in choosing the doses for in vivo research as well as providing preliminary data on the safety profile of a medication candidate.

After the formulation and evaluation of anti-diabetic herbal formulation, it has been expected that we are able to use it commercially and in the public welfare.

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